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Title: Moderators of the Effect of Psychological Interventions on Depression and Anxiety in Cardiac Surgery Patients: A Systematic Review and Meta-analysis.

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Abstract: Cardiac surgery patients may be provided with psychological interventions to counteract depression and anxiety associated with surgical procedures. This systematic review and meta-analysis investigated whether intervention efficacy was impacted by type of cardiac procedure/ cardiac event; control condition content; intervention duration; intervention timing; and facilitator type. MEDLINE, EMBASE, and PsycINFO were searched for randomized controlled trials comparing anxiety and depression outcomes, pre and post psychological and cardiac interventions. Twenty studies met the inclusion criteria for the review (N=2229) and 15 of those were meta-analyzed (N=1851). Depression and anxiety outcomes were reduced more when interventions were delivered after the cardiac procedure, when the controls offered some psychological content; and in patients receiving the 'longer' interventions. Anxiety (but not depression) was reduced most when interventions were delivered by a trained psychologist, and in implantable cardioverter defibrillator patients. Depression (but not anxiety) was reduced most in coronary artery bypass graft patients. In addition to estimating efficacy, future work in this domain needs to take into account the moderating effects of intervention, sample, and study characteristics.

Dear G.T. Wilson and Editorial Team,

Please, receive our manuscript titled: "Moderators of the Effect of Psychological Interventions on Depression and Anxiety in Cardiac Surgery Patients: A Systematic Review and Meta-analysis", by Cleo Protogerou, Nigel Fleeman, Kerry Dwan, Marty Richardson, Yenal Dundar, and Martin S. Hagger.

This study: (a) assessed the efficacy of psychological interventions to reduce anxiety and depression in cardiac surgery patients (e.g., implantable cardioverter defibrillator, coronary artery bypass graft); (b) investigated the moderating influence of intervention, study, and sample features (e.g., timing and duration of intervention, type of facilitator and control condition content); (c) discussed the relevance of the findings for practice and research. The focus of this study on subgroup analyses substantially adds to the literature, as previous reviews in this domain have overlooked or downplayed the impact of moderators on intervention efficacy.

In Word format, the manuscript is 25 pages long (inclusive of title page, abstract, and references, but excluding tables, figures and online supplementary material). The supplement includes the forest plots generated by primary, subgroup and sensitivity analyses, as well as results of a complete search strategy. The manuscript adheres to the 6th edition of the APA publication manual, and the Meta-Analysis Reporting Standards (MARS).

We confirm that this manuscript is not currently under review, submission, or publication elsewhere. All authors have read and approved this manuscript and agree with its submission to Behaviour Research and Therapy. The authors declare that they have no conflict of interest.

We look forward to hearing from you,

The Authors

Highlights

- Depression and anxiety outcomes were reduced more in post-surgery interventions.
- Depression and anxiety were reduced more if controls offered psychological content.
- Depression and anxiety were reduced more in ‘longer’ interventions.
- Anxiety alone was reduced most when psychologists delivered the interventions.
- Anxiety alone was reduced most in implantable cardioverter defibrillator patients.
- Depression alone was reduced most in coronary artery bypass graft patients.

Title

Moderators of the Effect of Psychological Interventions on Depression and Anxiety in Cardiac Surgery Patients: A Systematic Review and Meta-analysis.

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Abstract

Cardiac surgery patients may be provided with psychological interventions to counteract depression and anxiety associated with surgical procedures. This systematic review and meta-analysis investigated whether intervention efficacy was impacted by type of cardiac procedure/ cardiac event; control condition content; intervention duration; intervention timing; and facilitator type. MEDLINE, EMBASE, and PsycINFO were searched for randomized controlled trials comparing anxiety and depression outcomes, pre and post psychological and cardiac interventions. Twenty studies met the inclusion criteria for the review ($N=2229$) and 15 of those were meta-analyzed ($N=1851$). Depression and anxiety outcomes were reduced more when interventions were delivered after the cardiac procedure, when the controls offered some psychological content; and in patients receiving the 'longer' interventions. Anxiety (but not depression) was reduced most when interventions were delivered by a trained psychologist, and in implantable cardioverter defibrillator patients. Depression (but not anxiety) was reduced most in coronary artery bypass graft patients. In addition to estimating efficacy, future work in this domain needs to take into account the moderating effects of intervention, sample, and study characteristics.

Keywords: depression and anxiety; cardiac surgery patients; psychological interventions; evidence synthesis; moderator effects.

Coronary heart disease (CHD) is the leading cause of morbidity and death, globally (Hoyert & Xu, 2012; WHO, 2011). CHD treatment varies from taking medication and modifying behavior, to invasive cardiac procedures that usually include catheterisation, implantation of battery-operated devices, and open-heart surgery. Overall, the literature suggests that invasive cardiac procedures improve patient physical health and functioning. As a consequence, research has focused on evaluating patients' psychological well-being (Ai, Park, Huang, Rodgers, & Tice, 2007; Denollet, Schiffer, & Spek, 2010; Pedersen & Denollet, 2006; Škodová et al., 2009). While the literature suggests that cardiac surgery patients experience better psychological well-being post-surgery (Höfer et al., 2005; Shephard & Franklin, 2001), a substantial subgroup of these patients (approximately 20% to 30%) report a deterioration of physical functioning and increased psychological distress (Hawkes & Mortensen, 2006; Škodová, et al., 2009).

Patients who have undergone, or, are about to undergo, invasive cardiac procedures have been shown to be prone to high levels of distress. For example, up to 87% of implantable cardioverter defibrillator (ICD) patients may experience some degree of anxiety, while up to 38% of those patients may experience symptoms compatible to anxiety disorder (Bostwick & Sola, 2007). In addition, 15-20% of myocardial infarction (MI) patients experience symptoms of major depression (Hanssen, Nordrehaug, Eide, Bjelland, & Rokne, 2009; Thombs et al., 2006). In order to counteract depression and anxiety associated with cardiac procedures, cardiac patients may be provided with psychological interventions. Previous meta-analyses have investigated the efficacy of such interventions in reducing post-operative anxiety and depression in cardiac patients, and have yielded inconclusive results. For example, Dusseldorp, van Elderen, Maes, Meulman, and Kraaij (1999) found no benefit of 'psycho-educational' programmes on patient anxiety and depression, whereas Whalley, Thompson, and Taylor (2014) found significant benefits. Inconsistent results across meta-

analyses may be due, in part, to variability in study foci, outcome variables, and patient population included, making generalizations of findings difficult. For instance, van Dixhoorn and White (2005) included only myocardial ischaemia patients, while Whalley et al.(2014) excluded ICD patients and Linden, Phillips, & Leclerc (2007) primarily focussed on mortality and morbidity outcomes. An additional limitation of existing meta-analyses is the lack of subgroup analyses (moderator effects), even though the included psychological interventions are heterogeneous (Whalley et al., 2011). Concerns have also been raised (Thompson & Ski, 2013) as to what constitutes a ‘psychological’ intervention. This is an important concern given that some previous meta-analyses (Rees, Bennett, West, Davey, & Ebrahim, 2004; Welton, Caldwell, Adamopoulos, & Vedhara, 2009) have not made distinctions between psychological and non-psychological (e.g., physiotherapy, exercise, massage) components, making it thus difficult to isolate benefits solely attributable to the psychological components (Whalley et al., 2014). A clear understanding of intervention effects is more likely to be accomplished by isolating specific parameters impacting outcomes, which can reflect the possible underlying mechanisms through which effects are obtained (Michie, 2008).

This systematic review and meta-analysis aimed to add to the existing literature on the effectiveness of psychological interventions to reduce distress in cardiac patients and resolve some of the inconsistencies observed in previous meta-analytic syntheses of these data. Specifically, the current analysis aimed to (a) assess the efficacy of psychological interventions to reduce anxiety and depression in patients undergoing cardiac procedures; (b) explore the impact of intervention, study, and sample features on intervention efficacy, i.e., moderators of outcomes; (c) inform practice and research. The current review aimed to make an original contribution to the literature by identifying the moderating factors that diminish and magnify the effects of interventions on distress reduction in cardiac patients, a limitation

of previous meta-analyses and may account for the inconsistencies in the observed effect sizes across the reviews.

Methods

Clarification of Constructs

An important initial step in identifying the impact of psychological interventions on cardiac patients' distress was to adopt accepted criteria for the definition and operationalization of psychological interventions. In the current analyses, interventions had to be based on identifiable psychological theories or psychological techniques stemming from those theories (e.g., socio-cognitive theory, learning theory, psychodynamic). This inclusion criterion was adopted to ensure a level of quality control over the interventions in the studies included in the current analyses. We also stipulated that interventions were not to be combined with non-psychological (e.g., physiotherapy, massage, exercise) components likely to confound the effects of the psychological interventions. We use the term 'experimental intervention' to refer to the primary psychological intervention, and the term 'alternative intervention' to refer to a psychological intervention that was sometimes used as a comparator. We use the term 'distress' as a collective term for anxiety and depression (Mirowsky & Ross, 2002). We use the term 'moderators' to refer to intervention, study, and sample features, that were expected to affect the direction and/or strength of effect size estimates. Our meta-analysis focussed specifically on depression and anxiety outcomes, as measured by validated scales.

Eligibility Criteria

To be included, studies had to be randomised controlled trials (RCTs) that: (1) assessed the efficacy of a psychological intervention, as defined above; (2) were published from 1980 onwards; (3) included individuals aged 18 years or older, having undergone or were about to undergo an invasive cardiac procedure; (4) included measures comparing pre

and post intervention depression and anxiety by means of validated scales; (5) were published in the English language; and (6) were published full-text. Studies were excluded if they: (1) included ‘psychological’ interventions that deviated from the above definition; (2) psychological interventions aiming to modify outcomes other than psychological distress (e.g., morbidity, mortality, adherence to medication, exercise, bodily symptoms); (3) were duplicates of another RCT; (4) were abstract-only reports; and (5) did not measure depression and anxiety by means of a validated scale. We focus exclusively on RCTs as this design is considered to be the ‘gold standard’ used to establish the efficacy of health-related interventions (Norman & Streiner, 1993). The year 1980 was chosen as the earliest date for studies since the first ICD transplantation took place then, and rehabilitation programmes comprising psychological components for this patient group were subsequently developed. We included studies of patients who had undergone, or were about to undergo, a cardiac procedure as we wanted to assess whether the timing of the intervention, relative to the cardiac procedure, would impact anxiety and depression outcomes. Studies measured depression and anxiety pre and post psychological and cardiac intervention. Inclusion was restricted to studies utilizing validated to enhance accuracy and comparability of findings.

Search Strategy

We conducted an exhaustive search of electronic databases including MEDLINE, MEDLINE In-Process and Other Non-Indexed Citations, PsycINFO and EMBASE for the period from 1980 to July 2013. We also searched the reference lists of identified studies and Google Scholar. An updated search was conducted in June 2014, without yielding additional studies. Search terms for electronic databases included a combination of index terms (e.g., types of cardiac and vascular invasive surgical procedures) and free text words (e.g., psychological interventions) combined with specific conditions (e.g., depression, anxiety, emotional or psychological distress). A number of authors were contacted, via email, in order

to obtain additional information not reported in the published RCTs. Twenty RCTs met the inclusion criteria for the systematic review and 15 of those provided data suitable for the meta-analysis. Study selection and reasons for exclusion are presented in a flow chart (figure 1) based on PRISMA guidelines (Moher, Liberati, Tetzlaff, Altman, & Group, 2009). Two independent coders screened the abstracts for eligibility (stage 1 inclusion), then the full copies of eligible titles were independently screened using a priori inclusion-exclusion criteria, and then, the final list of included studies was identified (stage 2 inclusion). Disagreements about study inclusions were resolved by discussion and by consulting with a third coder. There were no geographical or publication outlet restrictions. The results of a complete search strategy are available online.

Data Extraction

A coding form was developed specifically for this meta-analysis, based on recommendations by (Lipsey & Wilson, 2001). The coding form captured: (a) study level descriptors (e.g., publication year, type, and location); (b) study sample descriptors (e.g., sample size, age, gender, type of cardiac procedure undertaken); (c) experimental and alternative intervention descriptors (e.g., duration, setting, medium, facilitator type); and (d) effect size level descriptors (e.g., outcome category, scales used, means, medians, standard deviations, sample sizes at appropriate measurement times). The coding form was independently pilot-tested by two coders (CP, NF) using 25% of the eligible studies, and inter-coder disagreements were resolved through discussion. All eligible studies were then coded independently by two coders and once again, disagreement was resolved through discussion.

Data Preparation and Analyses

Change from baseline in depression and anxiety was the primary outcome variable. The standardized mean difference (Hedges' g ; Hedges & Olkin, 1985) was the chosen effect

size metric for the intervention effect as different scales were used within the studies. Change from baseline difference was within-groups (i.e., the same distress outcome measures were obtained before and after the intervention for all groups), but the differences reported were between-groups (i.e., comparisons were made for intervention versus control groups). The 95% confidence intervals of the effect size were also computed. Where the studies did not report the standard deviation (SD) for change from baseline, this was calculated according to accepted guidelines (Higgins & Green, 2008, p. 488). To illustrate, the values $r = .50$ and $r = .70$ represent the range reported in one of the studies (Sorlie, Busund, Sexton, Sexton, & Sorlie, 2007). In this instance, the middle value of $r = .60$ was chosen for primary analyses, and sensitivity analyses (i.e., exploration of whether main findings change by varying aggregation method) were conducted using the upper and lower bounds of the correlation coefficient. This was to ensure that the selection of the center value was appropriate.

Outcome measures were summarized at post-intervention (earliest measurement taken after the psychological intervention) and follow-up (earliest measurement taken three months or more after the psychological intervention). The included RCTs compared at least two of the following conditions: experimental intervention, alternative intervention, and usual care control. Thus, outcomes were separately compared between the experimental intervention and usual care control conditions, as well as the experimental and alternative intervention conditions. Heterogeneity was assessed with the I^2 index, which offers the percentage of the variability in effect estimates due to heterogeneity rather than sampling error. I^2 values of .25), .50, and .75 translate to low, moderate, and high levels of heterogeneity, respectively (Higgins & Thompson, 2002). Risk of bias (i.e., threat to internal validity) was assessed using the Cochrane Collaboration's risk-of-bias tool (Higgins & Green, 2008). The risk-of-bias tool evaluates selection bias, performance bias, withdrawal/attrition bias, detection bias, and reporting bias. Due to the nature of the interventions, assessing blinding of treatment

assignment was not appropriate. In addition to assessing risk of bias separate domains, we created an overall (un-weighted) risk of bias score, by assigning to each domain a score of 1 for low risk of bias, 2 for unclear risk of bias, and 3 for high risk of bias, and summing these. An ‘overall low’ risk of bias estimation was given to studies that scored ≤ 6 ; an ‘overall unclear’ risk of bias estimation was given to studies that scored between 7-12; and an ‘overall high’ risk of bias estimation was given to studies that scored ≥ 12 . Two reviewers assessed all risk of bias studies independently and discrepancies were resolved through discussion. Risk of bias figures were created with Review Manager (RevMan, version 5.2) software. Possible asymmetries in the distribution of effect sizes, as an indicator of possible publication bias, were analyzed with the Egger et al.’s test (Egger, Davey Smith, Schneider, & Minder, 1997). A random effects model of meta-analysis was used because simulation data using this model suggest that it will provide the most robust estimates under conditions of high heterogeneity (DerSimonian & Laird, 1986). Studies were grouped and analysed separately to assess the impact of the following five moderators on the intervention effect: (1) type of cardiac procedure/cardiac event (CABG, ICD, other); (2) control condition content (usual care only; usual care plus additional content; usual care including a brief form of intervention; other); (3) intervention duration (short/up to one week, medium/up to six weeks, long/over six weeks, not reported); (4) facilitator type (trained psychologist, other trained health professional, student); and (5) timing of psychological intervention (before or after the cardiac procedure). These features were chosen as authors of previous studies have identified them as potential moderators of the psychological intervention-distress reduction relationship (Sears et al., 2007).

Results

Description of Studies

Studies sampled 2229 cardiac patients who were predominately male (75% of studies), and with mean ages between 56.10 and 68.70 for the intervention groups, 58.40 and 68.0 for the control groups, and 57.65 and 64.30 for the alternative intervention groups. Most studies were conducted in the United States ($k = 13$, 65%). Sample sizes varied from 30 to 246. Nine (45%) studies included only CABG patients, six studies (30%) included only ICD patients, and five studies (25%) included patients who had had one or another type of cardiac procedure/event. Thirteen studies (65%) used technology (i.e., audiotapes, video tape, compact disc/computer, and telephone) as the mode of intervention delivery. Fifteen studies (75%) included a usual care-only control condition as a comparator, while two (10%) studies provided only an alternative intervention as comparator and four (20%) studies offered an alternative intervention in addition to the control. Eleven interventions (55%) could be characterized as ‘long term’, as they were delivered for a minimum of six weeks, five interventions (25%) lasted up to 6 weeks (‘medium term’), and two interventions (10%) lasted up to one week (‘short term’). We were unable to ascertain the length of two interventions (10%), despite contacting authors. Maximum follow-up periods varied, from one week to two years. Half (50%) of the studies used a six-month follow-up measure. Most interventions were delivered at a hospital setting (even if there were follow-up sessions at the patient’s home) ($k=13$, 65%), and eleven (55%) were delivered by trained health professionals (usually nurses), one was delivered by a trained peer volunteer (5%), three were self-delivered (15%), and five (25%) were delivered by psychologists. The Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) and the Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983), were utilized in seven (35%), and five studies (25%) respectively. Anxiety was mostly measured using the State-Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) and the HADS, in seven (35%) and five (25%) studies, respectively. Finally, most interventions

($k=15$, 75%) were based on cognitive-behavior or social learning theory (Bandura, 1977), utilizing techniques, such as identifying and reframing negative thoughts; identifying and dealing with stressful situations; coping strategies; setting personal goals and ways of achieving those goals; group discussions with emphasis on group support; guided imagery; and stress reduction - relaxation techniques. While the remaining interventions ($k=5$, 25%) were labelled as types of counselling, support, or stress management programmes, they too incorporated cognitive behaviour techniques. Thus, based on our coding, we concluded that all included psychological interventions were based on cognitive-behavior theory principles and techniques. Table 1 provides a summary of included study characteristics and findings.

Risk of Bias in Included RCTs

For at least half of the included studies ($k = 11$, 55%) overall risk of bias was unclear. For two studies (10%) overall risk of bias was deemed low and for seven studies (35%) risk of bias was assessed to be high. The kappa statistic for the overall risk of bias was 0.72 (95% CI: 0.43, 1.00), indicating substantial agreement between the two assessors. Most studies clearly reported randomization procedures reflecting adequate random sequence generation ($k = 15$, 75%), whereas the remaining studies did not report full details of randomization procedures. Allocation concealment was unclear for most studies ($k = 13$, 65%), and only five studies (25%) clearly reported the method used to conceal the allocation sequence. Four studies (20%) reported that outcome assessors were blinded to group allocation. About half of studies ($k = 9$, 45%) indicated that data were either not missing or that missing data were handled adequately (e.g., used intention-to-treat analyses); five of these studies used intention-to-treat analyses to deal with attrition. More than half of studies ($k = 11$, 55%) reported outcomes completely and accurately (e.g., studies presented pre-specified outcomes, reported in full detail). Thus, the strongest methodological areas of included RCTs related to

randomization procedures and data reporting, while the weakest methodological area related to handling of missing data. Figures 2 and 3 depict authors' risk of bias assessment.

Quantitative Analyses

We tested out main hypotheses by applying random-effects meta-analysis to data on the effect of psychological interventions on post-surgery indices of distress, i.e., depression and anxiety across the sample of studies.

Change in depression and anxiety. Fifteen studies reporting data for depression and twelve studies reporting data for anxiety ($N = 1851$) were meta-analyzed. Relative to controls, experimental interventions succeeded in reducing depression at post-intervention ($g = -0.84$, 95% CI: -1.32 to -0.35, $k=15$) and at follow-up ($g = -0.72$, 95% CI: -1.30 to -0.13, $k=9$). Similarly, interventions succeeded in reducing anxiety at post-intervention ($g = -0.62$, 95% CI: -1.04 to -0.21, $k=12$) and at follow-up ($g = -0.64$, 95% CI: -1.22 to -0.07, $k=7$). Relative to alternative interventions, experimental interventions did not significantly reduce depression or anxiety at post intervention or follow-up. Heterogeneity was high ($I^2 > .75$), suggesting that results varied more across studies than expected by sampling error alone, and that more complex analyses (i.e., moderator analyses) were indeed warranted. Depression and anxiety outcomes were still significantly reduced at both time points, after varying the correlation coefficient that was used in the calculation of the SD for change from baseline (i.e., sensitivity analysis). One study indicated a much larger intervention effect than the remaining studies (i.e., > 3 standard deviations away from the mean) and was treated as an outlier. By removing this study, the estimates of intervention effect were substantially affected but still able to significantly reduce depression at post-intervention ($g = -.37$, 95% CI: -.77, to -.02, $k = 15$), anxiety at post-intervention ($g = -.36$, 95% CI: -.62, to .09, $k = 11$), and anxiety at follow-up ($g = -.24$, 95% CI: -.41 to -.07, $k = 6$).

Forest plots of effect sizes of all meta-analyses - including sensitivity analyses - are available as online supplemental material. There were asymmetries in the distribution of the effect sizes, suggesting the possibility of publication bias (Egger et al.'s test [$t = -2.18, p = .04$]; ($t = -3.02, p = .01$)] for depression and anxiety, respectively.

Moderators of change in depression and anxiety. Post-intervention depression decreased more when the experimental intervention (a) lasted longer, i.e., over six weeks ($z = 2.50, p = .01$); (b) was delivered post-surgery ($z = 2.36, p = .02$); (c) was compared to an alternative intervention ($z = 12.37, p = .00001$). Depression at this time point decreased most for CABG patients ($z = 2.36, p = .02$). Depression at follow-up decreased more when the experimental condition was compared to usual care only ($z = 1.94, p = .05$). Anxiety (post-intervention; follow-up) was reduced more when the experimental condition: (a) lasted longer/over six weeks [$(z = 2.10, p = .04)$; ($z = 3.13, p = .002$)]; (b) was delivered after the cardiac procedure [$(z = 2.24, p = .03)$; ($z = 3.24, p = .001$)]; (c) was delivered by a trained psychologist [$(z = 3.59, p = .0003)$; ($z = 4.23, p < .0001$)]. Anxiety (post-intervention only) was reduced more when the experimental condition was compared to a brief psychological intervention ($z = 2.51, p = .01$), while at follow-up (only) it decreased most for ICD patients ($z = 2.71, p = .007$). Forest plots generated by moderator analyses are as online supplemental material.

Discussion

The current meta-analysis aimed to examine the efficacy of psychological interventions to attenuate anxiety and depressive responses in cardiac surgery patients. Importantly, the analysis is the first to examine the impact of specific study, sample, and intervention features as moderators of the effect of psychological interventions on distress in cardiac surgery patients. Consistent with previous reviews, the randomized controlled interventions included in our meta-analysis significantly decreased depression and anxiety

relative to controls, and these benefits were sustained for a minimum of three months. Effect sizes of depression and anxiety change were medium to large.

Interventions that ameliorated both depression and anxiety lasted longer, were delivered after the cardiac procedure and were compared with some type of intervention, usually interventions adopting education and counselling techniques. It therefore seems that intervention techniques can be more effective when delivered for at least six weeks, as compared to shorter times. It also appears that psychological interventions may have more of an impact when delivered post-cardiac surgery. The moderating effect of control condition content implies that providing usual care only, even if that comprises education and counselling, may not be enough to reduce distress. Current data therefore suggest that a separate psychological intervention can be a beneficial addition to usual care. The type of cardiac procedure undertaken appeared to influence depression and anxiety. CABG patients reported greater depression reduction than patients undergoing ICD and other procedures, while ICD patients reported greater anxiety reduction. There is evidence to suggest that, compared to anxiety, depression is more prevalent in CABG patients (Tully & Baker, 2012). ICD patients appear to be more prone to anxiety, with some evidence to suggest that ICD procedures may induce anxiety disorders, *de novo* (Sola & Bostwick, 2005). It is possible, therefore, that the interventions included in this meta-analysis were most effective for CABG patients who tend to suffer more depression. Facilitator type influenced anxiety alone. Anxiety decreased the most when interventions were delivered by a trained psychologist. While there is little doubt that the delivery of psychological interventions by trained health professionals can ensure better intervention outcomes (Roth & Pilling, 2004; (Whalley et al., 2011), it is unclear why, in the current meta-analysis, psychologists had an impact on anxiety outcomes, alone. We speculate that the type of techniques required for targeting depression

mirror more closely those provided by other trained professionals, whereas techniques targeting anxiety require more specific training to be efficacious.

Study Strengths and Limitations

The current meta-analysis is the first to look at specific moderator variables of the effect of interventions on distress in cardiac surgery patients that have not been accounted for in previous meta-analyses and systematic reviews, such as intervention timing. Precision and accuracy of results was enhanced given that studies were included if they delivered psychological content; obtained anxiety and depression measures via robust, validated scales; and offered enough information to explore moderator effects. Moreover, outcome measures were summarized across time, at baseline, earliest post intervention, and a minimum of three months' follow-up. Subsequent to the two types of sensitivity analyses, a significant intervention effect was obtained for depression and anxiety at post-intervention and follow-up. A further strength of the current analysis is the adoption of rigorous study search, identification, and classification procedures. Specifically, study search and was carried out by an information specialist (YD), data extraction and coding were conducted by experienced reviewers (CP, NF), and authors were contacted to obtain additional information. Using experienced searchers and coders, and adding a supplemental search component, substantially enhances reporting quality (Mullins, DeLuca, Crepaz, & Lyles, 2014). In addition, a risk of bias assessment of included RCTs was conducted, highlighting areas of methodological strength and weakness.

As is the case with all meta-analyses, our meta-analysis mirrors limitations of the included primary studies. Detail about intervention content was sometimes minimal in the RCTs, often without specifying which particular techniques and strategies were used or linked to better outcomes. Thus, although our findings suggest that psychological interventions guided by cognitive behavior theory do work, it is not possible to ascertain

which techniques and strategies work best. Similarly, the content of usual care comparison groups tended to be inadequately reported or was not always neutral. For example, in some cases, ‘usual care’ still meant that patients were exposed to some kind of treatment resembling the active intervention content. The ‘right’ type of control group is imperative in psychological interventions, as content of control condition can affect the effect size of the active intervention (Lindquist, Wyman, Talley, Findorff, & Gross, 2007). Detailed demographic information was often lacking in the included studies and most studies were conducted in countries in the US, with predominately male participants. Limited demographic detail precluded us from conducting moderation analyses with demographic variables, or generalizing to other countries or cultures. Despite extensive search of studies, we identified a small number of RCTs ($k = 15$). This may account for the absence of statistically significant outcomes when experimental and alternative conditions were compared. However, evidence of potential publication bias indicates that additional and relevant RCTs may exist but remain unpublished. Heterogeneity was high for depression and anxiety outcomes, a possible reflection of the multiple generative mechanisms underlying the ‘high distress – poor cardiac outcomes’ relationship (Whalley et al., 2011). Risk of bias was deemed low in just two studies, indicating poor methodological quality across studies. However, our overall risk of bias measure was rather crude and the lack of methodological detail reported in some studies limited our confidence gauging risk of bias.

Insights for Practice and Research

Results of our meta-analysis suggest that psychological interventions aiming to reduce anxiety and depression in cardiac surgery patients can benefit from (a) delivering psychological content for longer time periods - at least for six weeks; (b) considering patient characteristics relating to the cardiac procedure undertaken and tailor content appropriately; (c) considering the timing of the intervention relative to the cardiac procedure; (d) limiting

methodological biases; and (e) using trained psychologists as facilitators. Also, the results suggest that psychological interventions can be more effective than usual care in reducing depression and anxiety in cardiac surgery patients, even when usual care comprises education, counselling, or a brief form of the intervention. Thus, it may be worth investing in developing separate distress reduction interventions for this patient population. Finally, while cognitive behavior techniques appeared to be successful in ameliorating depression and anxiety, clearer descriptions of intervention content and delivery is needed. As interventions will utilize multiple techniques, it is important to know which techniques are the more effective. Knowledge of the effectiveness of specific techniques is important as it relates to the effectiveness, efficiency, and feasibility of distress-reduction interventions for cardiac patients (Salmoirago-Blotcher & Ockene, 2009). Given that multi-component interventions are more expensive and more challenging to deliver, the inclusion of ineffective components would unnecessarily ramp-up costs for little or no gain with respect to health outcomes.

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(*Asterisked citations are the included RCTs.)

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Table 1

Study Characteristics

Study	Number of participants at baseline	Cardiac procedure undertaken	Mean (SD) age and gender of participants	Country Setting Facilitator	Type of intervention and control	Type of distress: scale used [§]	Timing of distress measurement	Summary of findings: groups favoured by the intervention
Black et al. (1998)*	All = 60 IG = 30 CG = 30	Angina, MI, angioplasty or CABG patients	All = 60.2 (10.7) Male = 88%	United States Hospital Psychologist	IG: Variety of CBT (1-7 sessions) CG: Usual care	Depression: SCL-90-R	Baseline: Before psychological intervention. Post-intervention: End of psychological intervention. Follow-up: 3, 6, 9; 21 months.	Favoured IG: Significantly reduced depression at 6 months compared to CG.
Brown et al. (1993)*	All = 40 IG = 20 AG = 20	MI or CABG	IG: 63.55 (7.43) Male = 55% AG: 57.65 (7.82) Male = 90%	United States Hospital Psychologist	IG: Variety of CBT (12 x 1-hour sessions) AG: Support, empathy and warmth (12 x 1-hour sessions)	Depression: BDI	Baseline: Before psychological intervention. Post intervention: 0. Follow-up: 3, 9, and 15 months.	Favoured IG: Significantly reduced depression at 15 months compared to AG.
Colella (2009)*	All = 185 IG = 61 CG = 124	CABG	All: 63.53 (10.4) Male = 100% IG: 63.6 (9.93) CG: 63.4 (10.7)	Canada Home Peer volunteer	IG: Telephone peer support – with CBT elements. CG: Usual care	Depression: BDI-II	Baseline: Before psychological intervention. Post-intervention: 6 weeks. Follow-up: 12 weeks.	Favoured no group.

Study	Number of participants at baseline	Cardiac procedure undertaken	Mean (SD) age and gender of participants	Country Setting Facilitator	Type of intervention and control	Type of distress: scale used [§]	Timing of distress measurement	Summary of findings: groups favoured by the intervention
Dao et al. (2011)*	All = 100 IG = 48 CG = 49	CABG	All: 63.6 (15.3) Male = 78% IG: 62.8 (11.8) Male = 77% CG: 64.2 (11.9) Male = 79%	United States Hospital Psychologist	IG: Brief CBT. CG: Usual care.	Anxiety: STAI-Trait Depression: BDI-II	Baseline: At least 7 days before the scheduled operation, and prior to psychological intervention. Post-intervention: at end of intervention. Follow-up: 3 to 4 weeks after CABG.	Favoured IG: Significantly reduced anxiety and depression at 3 to 4 weeks compared to CG.
Doering et al. (2007)*	All = 15 IG = 7 CG = 8	CABG	IG: 58.6 (7.6) Male = 0% CG: 60.9 (19.4) Male = 0%	United States Home (post hospital discharge) Nurse	IG: CBT CG: Usual care	Depression: BDI	Baseline: Before hospital discharge and prior to psychological intervention. Post-intervention: 3 months. Follow-up: 6 months.	Favoured IG: Greater symptom reduction at 3 months compared to CG.
Dougherty et al. (2004)*	All = 168 IG = 84 CG = 84	ICD	IG: 63.0 (12.3) Male = 79.8% CG: 65.1 (12.2) Male = 73.8	United States Home Nurse	IG: CBT (8 weekly phone sessions) CG: Usual care	Anxiety: STAI Depression: CES-D	Baseline: At hospital discharge and prior to psychological intervention. Post-intervention: 1 month. Follow-up: 3 months.	Favoured IG: Significantly reduced anxiety at 3 months compared to CG but no significant difference in depression between groups at any time.

Study	Number of participants at baseline	Cardiac procedure undertaken	Mean (SD) age and gender of participants	Country Setting Facilitator	Type of intervention and control	Type of distress: scale used ^s	Timing of distress measurement	Summary of findings: groups favoured by the intervention
Dunbar et al. (2009)*	All = 246 IG = 85 AG = 83 CG = 78	ICD	All: 58.5 • (11.1) Male = 75% IG: 59.0 (10.6) Male = 82.9% AG: 58.0 (10.9) Male = 71.6% CG: 58.4 (12.0) Male = 70.1%	United States IG: Acute-care setting prior to hospital discharge and then in acute care setting. AG: Home. Nurse	IG: CBT and SMT group intervention. Booster session between the 4th and 5th months. AG: Telephone counselling intervention. Booster session provided between the 4th and 5th months. CG: Usual care	Anxiety: STAI-state Depression: BDI-II	Baseline: During hospitalisation and prior to psychological intervention. Post-intervention: 1 month. Follow-up: 3, 6, 12 months.	Favoured both IG and AG: Compared to CG, IG had significantly lower anxiety levels at 3 months; AG had significantly lower depression levels at 12 months.
Freedland et al. (2009)*	All = 123 IG = 41 AG = 42 CG = 40	CABG	IG: 62 (11) Male = 44% AG: 59 (10) Male = 50% CG: 61 (9) Male = 57%	United States Setting unclear Psychologist	IG: CBT (12 weeks) AG: SSM (12 weeks) CG: Usual care	Anxiety: BAI Depression: BDI	Baseline: Prior to psychological intervention and after cardiac procedure. Post-intervention: 3 months. Follow-up: 6 and 9 months.	Favoured IG and AG compared to CG: Significantly reduced depression in IG at 3 and 9 months, significantly reduced depression in AG at 3 months; significantly reduced anxiety in IG at 3, 6 and 9 months, significantly reduced anxiety in AG at 9 months); depression reduction was greater and more durable in the IG group at 3 and 9 months.

Study	Number of participants at baseline	Cardiac procedure undertaken	Mean (SD) age and gender of participants	Country Setting Facilitator	Type of intervention and control	Type of distress: scale used [§]	Timing of distress measurement	Summary of findings: groups favoured by the intervention
Furze et al. (2009)*	All = 204 IG: 100 CG: 104	CABG	IG: 64.25 (8.81) Male = 85% CG: 65.29 (8.51) Male = 76%	United Kingdom Home Nurse	IG: Brief CBT phone sessions (for 3-4 weeks). CG: Education and counselling intervention phone sessions (for 3-4 weeks)	Anxiety: STAI-state Depression: CDS	Baseline: Not specified. Post-intervention: 8 weeks prior cardiac procedure. Follow-up: 6 weeks, 3 and 6 months after cardiac procedure.	Favoured IG pre-operatively: Significantly reduced depression but not anxiety; no significant differences between groups post-operatively.
Gallagher et al. (2003)	All = 196	MI, CABG, angioplasty, or stable angina patients	IG: 67 (10) Male = 0% CG: 68 (12) Male = 0%	Australia Home, following introductory in-hospital session. Nurse	IG: Phone counselling with CBT. CG: Usual care	Anxiety: HADS Depression: HADS	Baseline: 1 to 2 days before hospital discharge and before psychological intervention. Post-intervention: 12 weeks.	Favoured no group.
Gortner et al. (1988)	All = 67 IG: 32 CG: 35	CABG and/or valve surgery patients	All: 61.5 (SD not reported) Male = 80.6% IG age groups: [30 to 50: 18.8% 51 to 69: 68.8% 70 to 77: 12.5%] Male = 81.3% CG age groups: [30 to 50: 5.7% 51 to 69: 74.3% 70 to 77: 20.0%] Male = 80.0%	United States Setting unclear Nurse	IG: CBT and family functioning. CG: Usual care	Anxiety: POMS Depression: POMS	Baseline: 1 day before surgery and prior to psychological intervention. Post-intervention: 3 months. Follow-up: 6 months.	Favoured CG at 3 months: Significantly more CG subjects reported a greater ability to tolerate emotional distress and anger but no significant differences between groups at 6 months.

Study	Number of participants at baseline	Cardiac procedure undertaken	Mean (SD) age and gender of participants	Country Setting Facilitator	Type of intervention and control	Type of distress: scale used [§]	Timing of distress measurement	Summary of findings: groups favoured by the intervention
Hermele (2007)*	All = 56 IG = 20 AG = 17 CG = 19	CABG	All: 66.13 (SD not reported) Male = 69.6%	United States Home (prior to surgery) and intra-surgery at university hospital Self-delivered	IG: Guided imagery audiotape AG: Music therapy audiotape CG: Usual care	Anxiety: HADS Depression: HADS	Baseline: Before surgery and prior to psychological intervention) Post-intervention: 1 week.	Favoured IG and AG over CG: Significantly reduced anxiety at 1 week but no difference in depression between groups.
Kohn et al. (2000)	All = 49	ICD	All: 66 (10) Male = 65%	United States Hospital PhD-level psychology student	IG: CBT CG: no CBT	Anxiety: STAI Depression: BDI-II	Baseline: Before psychological intervention. Post-intervention: 9 months.	Favoured IG: Significantly reduced anxiety and depression in ICD recipients at 9 months in IG compared to CG, particularly among patients receiving shocks. Favoured no group
Kuhl (2007)*	All = 30 IG = 15 CG = 15	ICD	IG: 56.1 (15.1) Male = 62% CG: 58.7 (12.1) Male = 56%	United States Hospital Self-delivered	IG: CD-ROM containing a computerised CBT program. CG: Waiting treatment group	Trait anxiety: STAI-trait	Baseline: Before psychological intervention). Post-intervention: 1 month.	
Lewin et al. (2009)*	All = 192 IG = 71 CG = 121	ICD	IG: 58.7 (13.3) Male = 74% CG: 63.4 (12.1) Male = 83%	United Kingdom Home and 'while they were awaiting implantation'. Trained health professional	IG: Brief home-based, phone delivered CBT. CG: Usual care	Anxiety: HADS Depression: HADS	Baseline: Peri-implantation and 3 months before psychological intervention Post-intervention: 6 months.	Favoured IG: Fewer cases of anxiety and depression, up to 6 months of measurement but result did not reach statistical significance.

Study	Number of participants at baseline	Cardiac procedure undertaken	Mean (SD) age and gender of participants	Country Setting Facilitator	Type of intervention and control	Type of distress: scale used ^s	Timing of distress measurement	Summary of findings: groups favoured by the intervention
Lie et al. (2007)*	All = 203 IG = 101 CG = 102	CABG	IG: 62 (SD not reported) Male = 90% CG: 62 (SD not reported) Male = 89%	Norway Home Nurse	IG: Face-to-face, home-based informational and psychological support – some CBT elements. CG: Usual care	Anxiety: HADS Depression: HADS	Baseline: before surgery and prior to psychological intervention. Post-intervention: 6 weeks. Follow-up: 6 months.	In a predefined subgroup of patients with anxiety and/or depression symptoms at baseline, intervention significantly reduced anxiety and depression in IG compared to CG at 6 months.
Sears et al. (2007)	All = 30	ICD	All: Male = 70% IG: 60.27 (4.56) AG: 59.35 (2.62)	United States Hospital Trained health professional	IG: 6-week CBT. AG: Condensed version of IG.	Anxiety: STAI Depression: CES-D	Baseline: Prior to psychological intervention) Post-intervention: 2. Follow-up: 4 months.	Favoured IG: Significantly reduced anxiety in both groups but anxiety scores decreased more rapidly in IG. A significant increase in depression scores was observed in AG at 4 months.
Sorlie et al. (2007)*	All = 109 IG = 55 CG = 54	CABG	IG: 59.0 (5.4) CG: 57.5 (3.3) Gender not reported	Norway Hospital and home-based Nurse	IG: 12 min video plus two 40 min patient-centred session – with CBT techniques. CG: Usual care	Anxiety: BAI Depression: Zung	Baseline: Before intervention. Post-intervention: at discharge. Follow-up: 2 and 6 weeks; 6 months; 1 and 2 years.	Favoured IG: Significantly reduced anxiety from discharge and up to 1 year of measurement compared to CG; significantly reduced depression from 6 months to 2 years of measurement.

Study	Number of participants at baseline	Cardiac procedure undertaken	Mean (SD) age and gender of participants	Country Setting Facilitator	Type of intervention and control	Type of distress: scale used [§]	Timing of distress measurement	Summary of findings: groups favoured by the intervention
Stein et al. (2010)*	All = 56 IG = 20 AG = 17 CG = 19	CABG	IG: 68.7 (8.7) Male = 55% AG: 64.3 (1.4) Male = 58.8% CG: 65.4 (11.0) Male = 94.7%	United States Home (prior to surgery) and intra-operatively at hospital Self-delivered	IG: Guided imagery audiotape – CBT elements AG: Music audiotape CG: Usual care	Anxiety: POMS Depression: POMS	Baseline: Before CABG and before psychological intervention. Post-intervention: 1 week. Follow-up: 6 months.	Favoured no group
Trzcieniecka and Steptoe (1996)*	All = 100 IG = 50 CG = 50	MI and CABG	IG: 59.4 (7.7) Male = 86% CG: 61.0 (6.7) Male = 88%	United Kingdom Hospital and home Psychologist	IG: Relaxation-based stress management – with CBT elements. (10 weeks) CG: Usual care	Anxiety: HADS Depression: HADS	Baseline: Before psychological intervention Post-intervention: 6 months.	Favoured IG: Significantly reduced anxiety but not depression over time in IG compared to CG.

Note. BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory–II (updated version of BDI); CABG = Coronary artery bypass graft; CBT = Cognitive Behavioural Theory/Techniques; CES-D = Centers for Epidemiologic Studies-Depression; CG = Control group; HADS = Hospital Anxiety and Depression scale; ICD = Implantable cardioverter defibrillator; IG = Intervention Group (the primary intervention group when there are 2 compared); AG = Alternative intervention group; POMS = Profile of Mood States; SD = Standard deviation; SMT = Symptom management training; SSM = Supportive stress management; STAI = State-Trait Anxiety Inventory; STAI-state = State scale of STAI; STAI-trait = Trait scale of STAI.

* Study assessed and/or controlled for the existence of psychopathology at baseline (i.e., very high levels of distress, non-transient underlying conditions).

§ Studies may have used more than one measure; only the scales that were used for the meta-analyses are included here.

Studies in **boldface** were included in the meta-analysis.

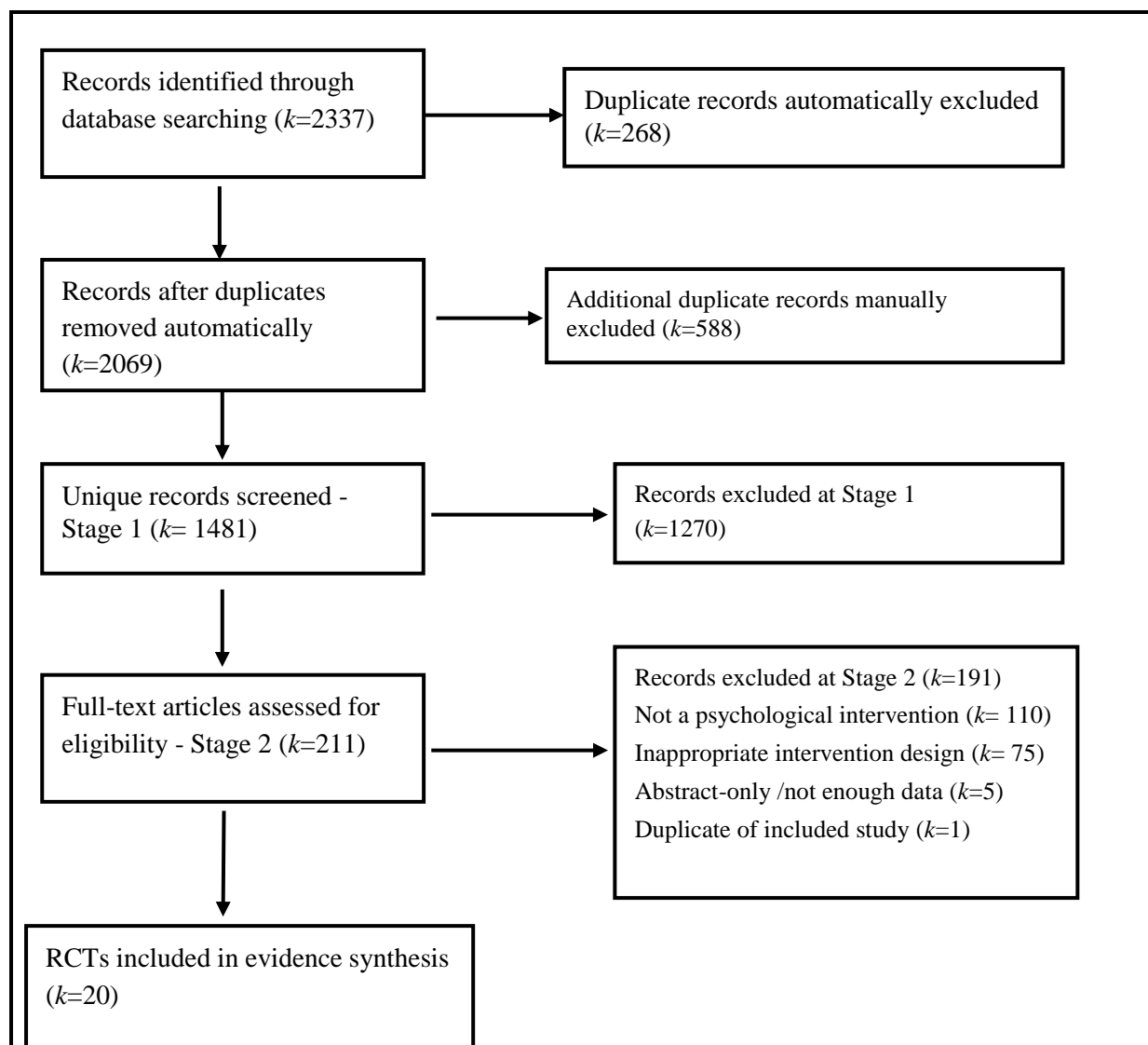


Figure 1. PRISMA flow chart.

Key reasons for excluding studies: (1) Not a psychological intervention: an intervention that was not guided by psychological theory and/or psychological techniques, or was an amalgamation of psychological and other components. If there was insufficient information to determine whether the intervention was psychological, then the intervention was excluded; (2) Inappropriate intervention design: an intervention that was not a RCT, and/or did not measure anxiety and depression by means of an objective/validated scale; (3) Abstract only/ not enough data: a paper that could only be obtained in abstract format and thus did not include enough data; (4) Duplicate of included study: study yielded no new data that was not contained in another publication.

Figure 2. Methodological quality summary: Review of authors' judgements about each methodological quality item presented as percentages of all included studies

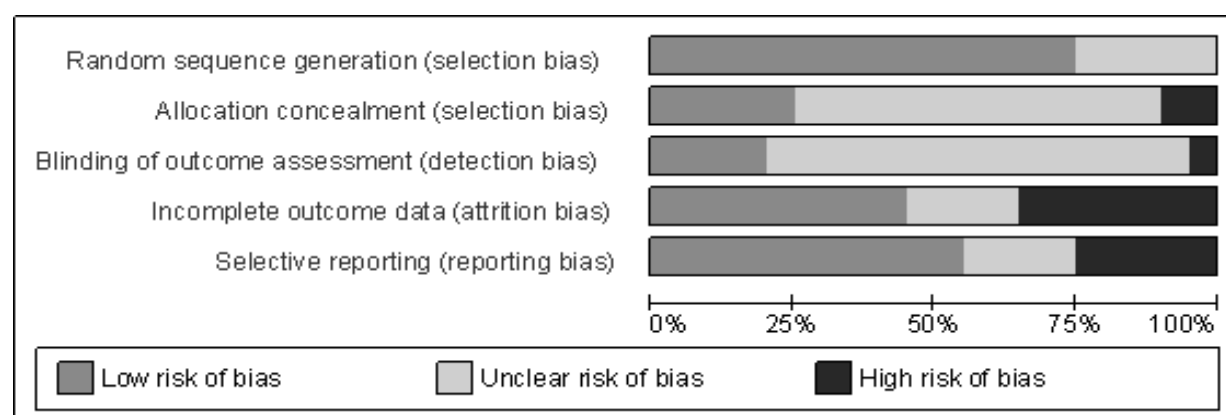


Figure 3. Methodological quality graph: Authors' judgements of each methodological quality item for each included study

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)
Black et al 1998	?	?	?	-	-
Brown et al 1993	?	?	?	-	+
Colella 2009	+	+	+	+	+
Dao et al 2011	+	?	?	+	?
Doering et al 2007	?	?	-	+	+
Dougherty et al 2004	+	?	?	+	+
Dunbar et al 2009	+	?	?	+	+
Freedland et al 2009	+	?	+	+	+
Furze et al 2009	+	+	+	?	?
Gallagher et al 2003	+	?	?	+	+
Gortner et al 1988	+	+	?	-	-
Hermele 2007	+	-	?	-	+
Kohn et al 2000	+	?	?	-	-
Kuhl 2007	+	?	?	-	-
Lewin et al 2009	+	?	?	?	?
Lie et al 2007	+	+	?	+	+
Sears et al 2007	?	?	?	?	-
Sorlie et al 2007	+	+	+	+	+
Stein et al 2010	+	-	?	-	+
Trzcieniecka et al 1996	?	?	?	?	?

Plus signs (+) indicate high methodological quality (low Risk of Bias); minus signs (-) indicate low methodological quality (high Risk of Bias); question marks (?) indicate unclear methodological quality (reported information about what happened in the study was insufficient).

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